~~37~~. (New) A pharmaceutical composition for use in the treatment of obesity in an animal, which comprises an effective amount of a peptide according to claim 16, together with one or more pharmaceutically acceptable carrier and/or diluents.

~~38~~. (New) A method of treatment of obesity in an animal, which comprises administering to the animal an effective amount of a peptide according to claim 16.

REMARKS

Applicants note the non-entry of the preliminary amendment filed March 7, 2001. The Examiner requests clarification with respect to the amendment filed July 20, 2001, particularly in terms of page reference and claim format. Applicants have amended the application according to the Examiner's request. Support for the amendments is found throughout the original specification, and no new matter is implicated.

Favorable reconsideration of the application is respectfully requested. The Examiner is invited to contact the undersigned, if it is felt this would advance the prosecution of the present application.

Respectfully submitted,

Date 8 May 2002 By S. A. Bent

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5109
Telephone: (202) 672-5404
Facsimile: (202) 672-5399

Stephen A. Bent
Attorney for Applicant
Registration No. 29,768

Mark-Up V rsion Showing Changes in the Specification

On page 6 at line 1:

The concept of correspondence in amino acid sequences between species is well known in the biological sciences and is determined by aligning comparable sequences (including if necessary theoretical deletions) to match isofunctional or isostereo amino acids thereby maximizing homology. The published corresponding sequences of the C-terminus region of the growth hormone of selected mammals are tabulated below[26], using standard single letter notation: (SEQ ID NOS 34-52, respectively in order of appearance)

On page 22 at line 4:

A. Synthesis of pentadecapeptide comprising amino acid residues 177-191 of native human growth hormone, designated as hGH (177-191) (Ref No. 9401): (SEQ ID NO: 1)

On page 25 at lines 22:

B. Synthesis of pentadecapeptide (Ref No. 9404): (SEQ ID NO: 7)

On page 25 at line 30:

C. Synthesis of the pentadecapeptide (Ref No. 9410): (SEQ ID NO: 12)

On page 26 at line 8:

D. Synthesis of the pentadecapeptide (Ref No. 9405): (SEQ ID NO: 9)

On Page 26 at line 10:

Ch_3CO-Leu[1]-Arg-Ile-Val-Gln-Cys-Arg-Ser-Val-Glu-Gly-Ser-Cys-Gly-Phe[15] (cyclic disulfide) (SEQ ID NO: 8)

On Page 26 at line 21:

E. Synthesis of the dicyclo-pentadecapeptide (Ref No. 9408): (SEQ ID NO:11)

On page 30 at line 6:

Tyr-Leu-Arg-Ile-Val-Gln-Cys-Arg-Ser-Val-Glu-Gly-Ser-Cys-Gly-Phe (cyclic disulfide) (SEQ ID NO: 19)

Mark-Up Version Showing Changes in the Claims

1. (Amended) A peptide which comprises an analogue of the carboxyl-terminal sequence of a growth hormone, said carboxyl-terminal sequence containing amino acid residues 177-191 of human growth hormone:

Leu-Arg-Ile-Val-Gln-Cys-Arg-Ser-Val-Glu-Gly-Ser-Cys-Gly-Phe (SEQ ID NO: 1),

or a corresponding sequence of a non-human mammalian growth hormone; wherein in said analogue

(i) amino acids at positions 182 and 189 of hGH are joined by a bond to promote a cyclic conformation; and/or

(ii) amino acids at positions 183 and 186 of hGH are joined by a salt bridge or a covalent bond;

or an organic or inorganic acid addition salt thereof.

13. (Amended) A peptide of the sequence:

X^1m-Leu-Arg-Ile-Val-Gln-Cys-Arg -Ser-Val-Glu-Gly-Ser-Cys-Gly-Phe-X^2n (SEQ ID NO: 2)

wherein X^1 and X^2 are each selected from the group consisting of L- or D- Arg, His, Lys and Tyr, and m and n are each 0, 1, 2 or 3 with the proviso that at least m or n is 1;

a cyclic disulfide thereof or an organic or inorganic acid addition salt thereof.

14. (Amended) A peptide of the sequence:

Y^1-Leu-Arg-Ile-Val-Gln-Cys-Arg-Ser-Val-Glu-Gly-Ser-Cys-Gly-Phe (SEQ ID NO: 3)

wherein Y^1 is selected from the group consisting of the desamino form (H), acetyl (CH_3CO-) and other acyl groups;

a cyclic disulfide thereof or an organic or inorganic acid addition salt thereof.

15. (Amended) A peptide of the sequence:

Leu-Arg-Ile-Val-Gln-Cys-Arg-Ser-Val-Glu-Gly-Ser-Cys-Gly-Phe-Y^2 (SEQ ID NO: 4),

wherein Y^2 is selected from the group of $CONH_2$ and alkyl amide groups;

a scyclic disulfide thereof or an organic or inorganic acid addition salt thereof.

16. (Amended) A peptide which is selected from the group consisting of

[Ref No.	STRUCTURE
9502	Leu Arg Ile Val Gln Pen Arg Ser Val Glu Gly Ser Pen Gly Phe
9405	CH_3CO- Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9410	H - Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9404	Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe - $CONH_2$
9407	Leu Arg Ile Val Gln Cys Lys Ser Val Glu Gly Ser Cys Gly Phe
9408	Leu Arg Ile Val Gln Cys Lys Ser Val Glu Gly Ser Cys Gly Phe |_____|(amide bond)
9604	Tyr Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Ph
9605	Lys Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9618	Lys Lys Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9607	Ala Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9606	Leu Lys Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9608	Leu Arg Ala Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9403	Leu Arg Lys Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9609	Leu Arg Ile Ala Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9610	Leu Arg Ile Val Ala Cys Arg Ser Val Glu Gly Ser Cys Gly Phe
9612	Leu Arg Il Val Gln Cys Arg Ala Val Glu Gly Ser Cys Gly Phe
9613	L u Arg Il Val Gln Cys Arg S r Ala Glu Gly Ser Cys Gly Phe

9615	L u Arg Ile Val Gln Cys Arg S r Val Glu Ala S r Cys Gly Phe
9616	Leu Arg Il Val Gln Cys Arg Ser Val Glu Gly Ala Cys Gly Ph
9602	Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Ala Phe
9501	Leu Arg Ile Val Gln Cys Arg Ser Val Glu D-Ala Ser Cys D-Ala Phe
9601	Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Ala]

Leu Arg Ile Val Gln Pen Arg Ser Val Glu Gly Ser Pen Gly Phe (SEQ ID NO: 15),

CH_3CO- Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 8),

H - Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 12),

Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe – $CONH_2$ (SEQ ID NO: 7),

Leu Arg Ile Val Gln Cys Lys Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 10),

Leu Arg Ile Val Gln Cys Lys Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 11),

|_____|(amide bond)

Tyr Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 19),

Lys Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 20),

Lys Lys Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 33),

Ala Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 22),

Leu Lys Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 21),

Leu Arg Ala Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 23),

Leu Arg Lys Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 6),

Leu Arg Ile Ala Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 24),

Leu Arg Ile Val Ala Cys Arg Ser Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 25),

Leu Arg Ile Val Gln Cys Arg Ala Val Glu Gly Ser Cys Gly Phe (SEQ ID NO: 27),

Leu Arg Ile Val Gln Cys Arg Ser Ala Glu Gly Ser Cys Gly Phe (SEQ ID NO: 28),

Leu Arg Ile Val Gln Cys Arg Ser Val Glu Ala Ser Cys Gly Phe (SEQ ID NO: 30),

Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ala Cys Gly Phe (SEQ ID NO: 31),

Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Ala Phe (SEQ ID NO: 17),

Leu Arg Ile Val Gln Cys Arg Ser Val Glu D-Ala Ser Cys D-Ala Phe (SEQ ID NO: 14),

Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Ala (SEQ ID NO: 16),

[wherein the amino acid residue abbreviations used are in accordance with the standard peptide nomenclature:

Gly = Glycine; Ile = Isoleucin ;

Glu	**=**	**Glutamic Acid;**	**Phe**	**=**	**Phenylalanin ;**
Cys	**=**	**Cysteine;**	**Arg**	**=**	**Arginine;**
Gln	**=**	**Glutamine;**	**Leu**	**=**	**Leucine;**
Ser	**=**	**Serine;**	**Val**	**=**	**Valine;**
Lys	**=**	**Lysine;**	**Ala**	**=**	**Alanine;**
Asp	**=**	**Aspartic acid;**	**His**	**=**	**Histidin**
Orn	**=**	**Ornithine;**	**Tyr**	**=**	**Tyrosine;**
Pen	**=**	**Penicillamine (β,β'-Dimethyl-Cysteine)]**			

wherein all amino acids, except for glycine, are of the L-absolute configuration, unless indicated as D-absolute configuration, and the peptide has a cyclic disulfide bond between Cys(182) and Cys(189) or Pen(182) and Pen(189) as appropriate, or an organic or inorganic acid addition salt thereof.

17. (Amended) A method for the treatment of obesity in an animal, which comprises administering to the animal an effective amount of a peptide according to claim 1 [any one of claims 1 or 7 to 16].

34. (Amended) A method according to claim 17 [or claim 18], wherein the peptide is administered orally.

36. (Amended) A pharmaceutical composition for use in the treatment of obesity in an animal, which comprises an effective amount of a peptide according to claim 1 [any one of claims 1 to 7 or 16], together with one or more pharmaceutically acceptable carriers and/or diluents.